# STUDIES ON THE CONDITIONS OF ACTIVITY IN ENDOCRINE GLANDS

## III. The Influence of the Adrenal Secretion on the Thyroid

BY
W. B. CANNON AND McKEEN CATTELL

*From the Laboratory of Physiology in the Harvard Medical School*

Reprinted from The American Journal of Physiology,
Vol. XLI, No. 1, July, 1916

WELLCOME INSTITUTE
LIBRARY
Coll. wellOmec
Coll. psm
No. WK 700
1916
C22s

Reprinted from The American Journal of Physiology, Vol. 41, No. 1,
July, 1916

# STUDIES ON THE CONDITIONS OF ACTIVITY IN ENDOCRINE GLANDS

## III. The Influence of the Adrenal Secretion on the Thyroid

W. B. CANNON and McKEEN CATTELL

*From the Laboratory of Physiology in the Harvard Medical School*

Received for publication April 27, 1916

One of the most interesting possibilities offered by the use of the action current as a sign of glandular functioning is that of testing assumed interrelations among the ductless glands. Of course, the effect of activity of one gland on the activity of another would have to be accomplished with reasonable rapidity in order to be demonstrated by the galvanometer. It is quite possible that the influence of some glands on others, such, hypothetically, as that of the ovary on the thyroid, might be so gradual in its development as not to be recognizable by an electrical change. The conditions might be different in other relations in which quick effects are produced. Thus the adrenal glands are known to respond promptly to stimulation, and their secretion is rapidly influential. The thyroid glands also are capable of ready action, as shown by the brief latent period of their response after sympathetic stimulation. Consequently if the adrenals are capable of exciting the thyroid bodies, the effects should be demonstrable by means of the galvanometer.

Because in their experiments injection of adrenin increased the basal protein metabolism in dogs—a condition the same as that seen in hyperthyroidism and the opposite of that produced by removal of the thyroid glands—Eppinger, Falta and Rudinger (1) declared that the adrenal medulla probably exerts a stimulating influence on the thyroid gland. Since stimulation of sympathetic fibers induces in the thyroid gland a marked electrical change, as the paper before this one demonstrates, and since adrenin everywhere in the body duplicates the action of sympathetic impulses, the suggestion that adrenin and adrenal secretion may stimulate thyroid secretion seems highly reasonable. It is a suggestion easily put to test.

Figure 1 is the record made by the action current of the thyroid when 0.1 cc. of adrenalin (1: 100,000)[1] was injected (at *a*) intravenously. After a latent period (which in different instances varied from about 10 seconds upwards) the galvanometer was sent out to +77 and at the end of five minutes had slowly returned to +7, when the drum was stopped. This result and many others like it, have proved clearly that adrenin has a striking effect on the thyroid gland.

In a previous paper we have presented evidence that the nerve impulses delivered to the thyroid by sympathetic fibers do not act by lessening the blood supply, but stimulate the gland cells directly (2). This evidence is further supported by such results as are illustrated in figure 1. The amount of adrenalin injected in that instance was such as to produce a fall in blood pressure (3)—an effect due to relaxation rather than to contraction of the arterioles. We are justified, therefore, on the basis of this consideration in connection with considerations previously adduced, in drawing the conclusion that the thyroid action current evoked by small doses of adrenin is an indication of secretory activity.

Fig. 1. Thyroid action current resulting from the intravenous injection of adrenalin (0.1 cc., 1: 100,000) at *a*. Time recorded on base line here and in other figures in half-minutes.

This conclusion accords with recent observations by Osokin (4) that adrenin injections produce marked histological changes in the cells of the thyroid—changes which he regards as of secretory rather than of pathological character. It is not in agreement with Wiener's inference (5) that adrenin leads to a storage of thyroglobulin in the gland. But this inference was based on only two cases, and the figures from these cases are so different as to make hazardous any conclusion

[1] During the course of this investigation some observations by Mr. D. L. Rapport and one of us (W. B. C.) led to the discovery that stronger solutions of adrenalin (e.g., 1: 10,000) would affect other than gland tissue and smooth muscle. Thus if the galvanometer is connected with the muscles of the thigh, an intravenous injection of adrenalin (0.5 cc., 1: 10.000) will cause the galvanometer to move out continuously in the direction which would be determined by increase of the compensating current (cf. Cannon and Cattell: This Journal, 1916, xli, pp. 44, 45. This effect is not produced, however, by injections of small amounts (0.1 to 0.5 cc.) of adrenalin in dilutions of 1 to 100,000—amounts, however, which excite sympathetic endings.

whatever. The evidences from increase of protein metabolism after adrenin injection, from the increased histological changes of thyroid cells after such injection, and from the concordance of the action currents produced by sympathetic stimulation and by adrenin, all point clearly to a direct secretory influence of adrenin on the thyroid.

The question now arises, can the secretion of the adrenal glands call forth an action current from the thyroid? The well proved power of splanchnic impulses to stimulate secretion from the adrenals makes simple an experimental testing of this question. We bared the splanchnic trunks low in the thorax, tied them together tightly at the upper end of the bared portion, crushed the nerves central to the ligature, and slipped beneath them shielded electrodes. Also a bit of twine was looped around the inferior vena cava, close to its entrance into the thorax, so that by a slight pull the blood could be prevented from re-

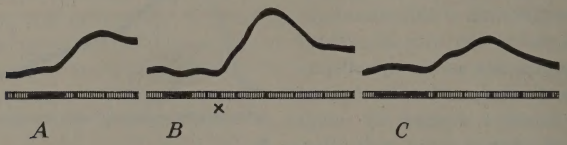
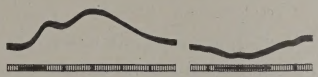



Fig. 2. *A*, 3.34. Thyroid action current resulting from splanchnic stimulation, 35 seconds. *B*, 3.42. The same, except that return of blood through the inferior cava was prevented from the beginning of stimulation (30 seconds) until a minute later (at *x*). *C*, 3.55. Thyroid action current on releasing blood from abdominal vena cava after restraining it one minute.

turning through this vein to the heart. Now with the leading-off electrodes in place on the thyroid gland and on neighboring subcutaneous connective tissue, and the galvanometer at zero, the splanchnic fibers below the ligature were stimulated by means of a weak induced current. The record of such an experiment is shown in figure 2. The record in figure 2 *A* is that resulting when the splanchnic nerves were stimulated (at 3.34) with a weak tetanizing current for 35 seconds. The latent period was about 23 seconds from the beginning of stimulation. In figure 2 *B* (3.42) the nerves were stimulated just as they were in the case of *A*, but blood was prevented from returning from the abdomen through the inferior vena cava by a pull on the loop about the vessel. This tension was maintained for a full minute after the start of stimulation. The thyroid action current instead of appearing about 23 seconds after the stimulus was applied to the nerves (as in *A*),

did not appear until the loop about the inferior cava was released (at $x$)—more than a minute after excitation was commenced. In all probability the higher rise in $B$ (to +45) compared with that in $A$ (to +30) is due to the action of some substance accumulated during the damming back of the blood in the abdomen. That retention of blood in the veins of the abdomen does not by itself produce the effects seen after splanchnic stimulation is shown by figure 2 $C$. In this instance the loop about the inferior cava was pulled upon for a minute (3.55), and then the accumulated blood was released. During the next minute the galvanometer moved slowly out to +22, and then slowly back to zero. The rise is only half as high as it was in $B$, when the same procedure was followed, but without stimulation of the splanchnics. Furthermore the maximum effects were reached nearly thirty seconds later in $C$ than in $B$.



*A* *B*

Fig. 3. *A*, 5.16. Thyroid action current following splanchnic stimulation, 30 seconds. *B*, 5.33. Absence of electrical effect on stimulating (for 60 seconds) the splanchnics after removal of the adrenal glands.

Splanchnic impulses may affect liver and pancreas as well as the adrenal glands. Discrimination of possible influences from these various sources is desirable. This can be done by noting the effect of splanchnic stimulation before and after removal of the adrenals. In figure 3 $A$ is shown the record of a thyroid action current resulting from the stimulation of the splanchnic nerves (at 5.16). The galvanometer moved to +18 and to +29 and returned to +5. The adrenal glands were then carefully removed and thereupon the splanchnics were stimulated again (at 5.33) for one minute. The only effect was a wandering of the galvanometer from 0 to −4, back to 0, and to +4, as shown in figure 3 $B$. Subsequent injection of adrenalin in this instance induced a characteristic electrical change.

From the evidence illustrated above we are justified in concluding that the amount of adrenal secretion liberated by splanchnic stimulation is sufficient to excite the thyroid gland in a manner similar to its excitation by sympathetic impulses and by adrenin injections. Obviously the efficiency of sympathetic impulses in provoking activity of the thyroid might be greatly augmented by the simultaneous secretion of the adrenal glands. It is significant, therefore, that both the thyroids and the adrenals would be simultaneously stimulated by the diffusely distributed impulses of sympathetic neurons.

In an earlier paper (6) attention has been called to the emergency function of the adrenal glands in times of emotional stress, as distinguished from a routine function. The thyroid, likewise, doubtless has a routine function—one that serves to keep metabolism normal. That function can probably not be investigated by electrical methods. Because the gland is subject to sympathetic impulses, however, and because it responds to stimulation with great promptness, probably it also has an emergency function—one that is exercised particularly in times of emotional crisis. It may be that such an emergency function is an exaggerated form of the routine activity of the glands, but the determination of these suggestions must be left to future researches.

SUMMARY

Injection of small doses of adrenalin (0.1 to 0.2 cc., 1: 100,000) evokes in the cat an action current of the thyroid gland.

Stimulation of the splanchnic nerves physiologically separated from the central nervous system likewise evokes an action current of the thyroid gland. This electrical change does not occur if the return of blood from the abdomen is prevented, but takes place promptly when the pent blood is released. The change also fails to appear after splanchnic stimulation if the adrenal glands have been previously removed.

REFERENCES

(1) Eppinger, Falta and Rudinger: Zeitschr. f. klin. Med., 1908, lxvi, 26, 28.
(2) Cannon and Cattell: This Journal, 1916, xli, 69.
(3) Cannon and Lyman: This Journal, 1913, xxxi, 385; Hartman: Ibid., 1915, xxxviii, 442.
(4) Osokin: Russkiy Vrach, 1915, xiv, 300.
(5) Wiener: Arch. f. exper. Path. u. Pharm., 1909, lxi, 313.
(6) See Cannon: This Journal, 1914, xxxiii, 356.

THE WAVERLY PRESS
BALTIMORE, U. S. A.